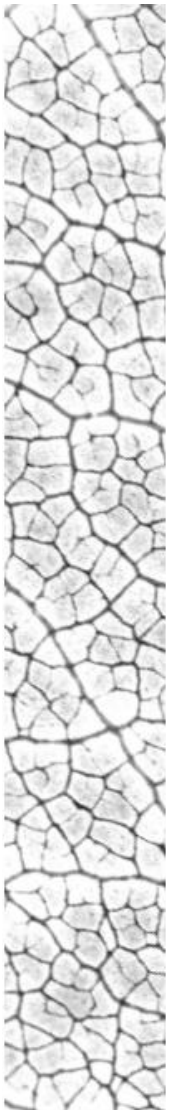

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The relation between maternal age with placental weight: Histological study

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Abstract
This study shows the effect of age of women on placental barrier thickness, fetal and placental weight. The work was done on total 25 human full term placentas of multiparous healthy pregnant women obtained from department of Obstetrics and Gynecology unit in Al-Zahra hospital in Najaf. The women in this work were classified into two groups; the control group consisted of 10 placentas from pregnant women between age of 20-34 years and experimental group consisted of 15 placentas from pregnant women of 35 years old and more. Stereological and histological studies were done to determine the effect of advanced maternal age on placental barrier and fetal and placental weight. The results showed: 1. Increase in the mean of placental barrier thickness of the placenta of mother > 35 years than that of placenta of control group (20-34 years). 2. Increase in the mean placental weight of mother > years in comparison to that of the control. 3. Decrease in mean birth weight of mothers > 35 years in comparison of that of the control. 4. Extensive morphological changes in the structural component of terminal villi (capillaries, stoma and trophoblast). The results showed that there is an increase in the placental barrier of placenta, decrease in vascularization of the terminal villi and increase in the stroma and fibrin deposition in the placenta of mothers more than 35 years of age regarding to normal group.

Keywords: stereology, histology¸ placenta, maternal age, stroma

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INTRODUCTION

The placenta is important for normal development of fetus and failure of placenta can result in big problems. The placental development is dependent upon the differentiation and invasion of the trophoblast (Shwan et al. 2005). Through this development of invasion and differentiation the trophoblast cells quickly separated to make contact between mother and fetus. As organs grow, the placenta expose to constant tissue remodeling, which is characterized by the functional loss of trophoblast cells by apoptosis. After proliferation and differentiation into specific cell subtypes, aging trophoblast cells are removed and replaced by younger trophoblast cells without affecting neighboring cells (Shwan et al. 2005). The important structures of the placenta are the chorionic villi within which the fetal blood is separated by only three cells layers (placental membrane) from maternal blood in the surrounding intervillous space (Gude et al. 2004). The capillaries are only the content of terminal villi.

The exchange of materials between fetus and mother happen at feto-maternal membrane which separates maternal blood in the intervillous space from fetal circulation (Shwan et al. 2005). The feto-maternal membrane is the most important part of the placenta. It is composed of vascular endothelial cells and their basement membrane, connective tissue of villous, sub-epithelial basement membrane and its covering of cyto and syncytiotrophoblast (Vogt 2001). The membrane which separate maternal and fetal blood allow water, O_2, nutrients and hormones to exchanges of mother to fetus and waste products from fetus to mother (Gude et al. 2004). The villi undergo changes according to development to occupy the demand of fetus (Hellstorm et al. 2001). The changes which occur in placental membrane have important effect on exchange between mother and fetus blood, and growth of fetus (Kingdom et al. 2000). As when placental function not efficient will effect on growth and development of fetus so lead to fetus with low birth weight and retarding of growth (Jaunlaux et al. 2000).

The best age for gestation is between 20 and 29 years, so any pregnancy above 35 years become at high risk for big complication like placental dysfunction

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(Miletic et al. 2002). Older maternal age is known as a risk factor for various types of obstetric complication including placental dysfunction. The age of the mother has an effect on the placental function during pregnancy and delivery (Hansen 1986). It has been well documented that the risks for premature delivery and fetal complications are higher in pregnancies of older women (Frettis et al. 1995). Pregnancy of aged women is associated with many factors including diabetes mellitus, hypertension, placenta brevia, premature rupture membrane, miscarriage risk, preterm delivery, and abruption placenta (Neal and More 2005). The placenta is important organ of pregnancy that help the normal growth and development of fetus. Growth and function of placenta are controlled and coordinated to perform the exchange of nutrients and west products between fetal and maternal blood barrier (Gude et al. 2004). In this research we assess the thickness of placental barrier in old age pregnancies regarding to young one.(Akinrotoye et al 2018, Anzaku et al 2017).

MATERIALS AND METHODS

This study was done on a total of 25 full term human placenta of multiparous healthy pregnant women. The samples were collected from the department of Obstetrics and Gynecology in Al-Zahraa hospital in Najaf. The samples of pregnant women classified into two groups according to maternal age at delivery. The control group consisted of 10 women between the age 20-34 years and the experimental group consisted of 15 women over 35 years old. Placental samples are collected. Fetal weight and placental weight were measured. Placental tissue samples were taken from various many of placenta. Placental tissue were fixed in 10% formalin for 24 hours, dehydration was done by using graded concentrations of alcohol. Clearing was done by using xylene, then embedding in paraffin. The samples then cut into thin sections 3-5 um. The sections then stained with haematoxylin and eosin (Clay 1971). Thickness of placental barrier of both control and experimental sections were measured by using Reichert Austria Nr381116 light microscope with screen.

Statistical Analysis

Data were analyzed statistically, using student's (*t* test) of significance and *p* value. The test was done between the two groups regarding the birth weight, placental weight and placental barrier thickness.

RESULTS

The main result is detailed in **Table 1** and in **Figs. 1**-**7**.

1. Placental barrier thickness: there is an increase in the mean of placental barrier thickness of the placenta of mothers age >35 years than that of placenta of control group (20-34) years. The difference is significant (p <0.01) as shown in (**Table 1**) and (**Fig. 1**).

Table 1. Shows a comparison between placenta of maternal age > 35 years of age and the control regarding placental barrier thickness, fetal and placental weight

Parameters	Maternal age > 35 years Mean± SD	Maternal age (20-34) years Mean± SD	*P Value*
Mean of placental barrier thickness in um	**4.44**±0.57	**2.30**±0.55	**P < 0.01**
Mean of placental weight in Kg.	**0.68**±0.012	**0.63**±0.021	**P < 0.01**
Mean of birth weight in Kg.	**3.27**±0.25	**3.42**±0.24	**P < 0.05**

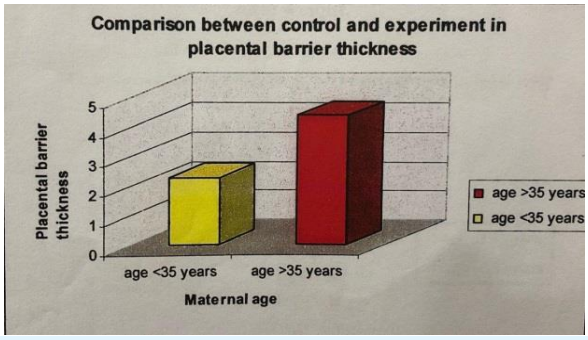

Fig. 1. Shows a comparison between the mother > 35 years of age and the control group in placental barrier thickness

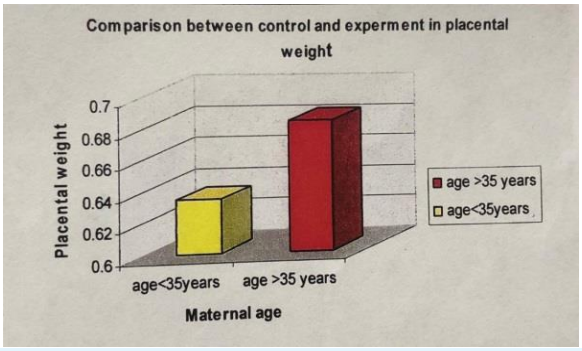

Fig. 2. Shows a comparison between the mother > 35 years of age and the control group in placental weight

2. Placental weight: the results showed that there is an increase in the main placental weight of mothers' age >35 years in comparison to that of the control (20-34 years). The mean placental weight is significantly greater in placentas of mother> 35 years than in placentas of control (20-34 years), as in (**Table 1**) and (**Fig. 2**).

3. Birth weight: the results showed that there is decrease in mean birth weight of mothers age > 35 years in comparison to that of control. The difference between the birth weight of the two groups was not significant (p> 0.05) as in **Table 1** and **Fig. 3**.

4. Morphological changes: the placenta of pregnant mother > 35 years of age showed extensive morphological changes in the structural component of terminal villi (capillaries, stroma and trophoblast). The results showed that there is an increase in the thickness of placental barrier of placenta of mother > 35 years of age in regarding to normal group as shown in **Figs. 4** and **5**. There id decrease in vascularization of the terminal villi (**Figs. 5** and **6**) and increase in stroma and

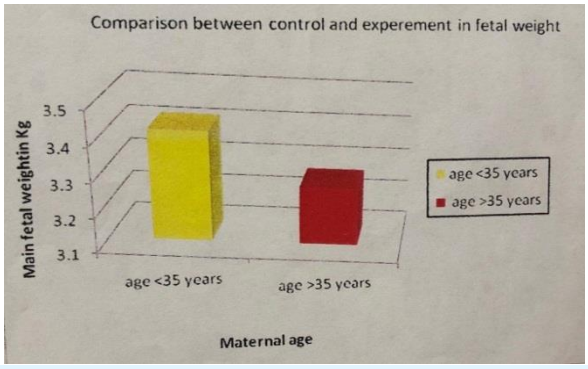

Fig. 3. Shows a comparison between the mother > 35 years of age and the control group in fetal weight

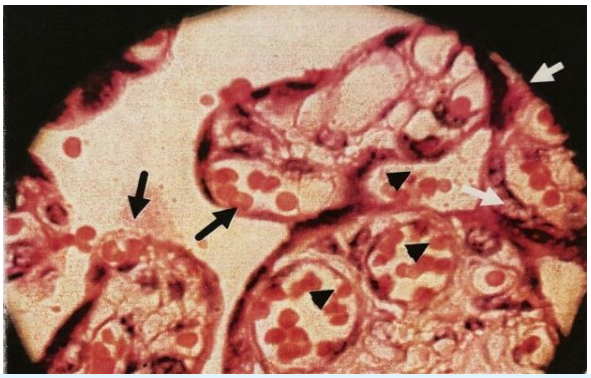

Fig. 4. Placenta of the control group shows thin placental barrier (black arrows) and synsytial knots (white arrows) and more villous capillaries (black head arrows). X1000

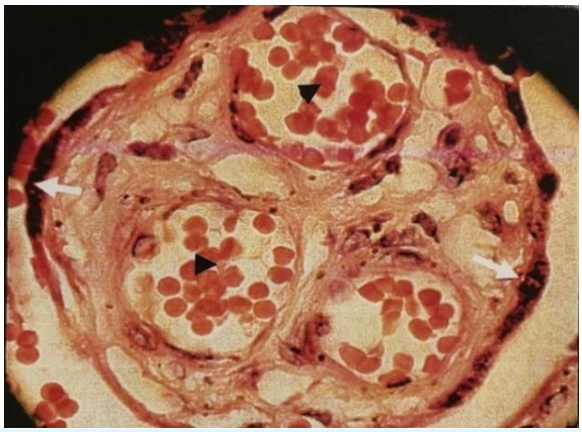

Fig. 5. Terminal villi of the placenta of the control group shows more villous capillaries (black head arrows) and more synsytial knots(white arrows). X1000

fibrin deposition in the placenta of mothers > 35 years of age in regarding to normal group as shown in (**Figs. 6** and **7**).

DISCUSSION

Placenta is a important organ which is very firmly connected to the mother but loosely connected to the developing fetus through umbilical cord organ providing interchange between mother and fetus. The life of fetus depends on welfare of the placenta and the life of

Fig. 6. Placenta of maternal age > 35 years shows stromal fibrosis (black arrows), small villous capillaries (white arrows), and thick placental barrier (black head arrows). X1000

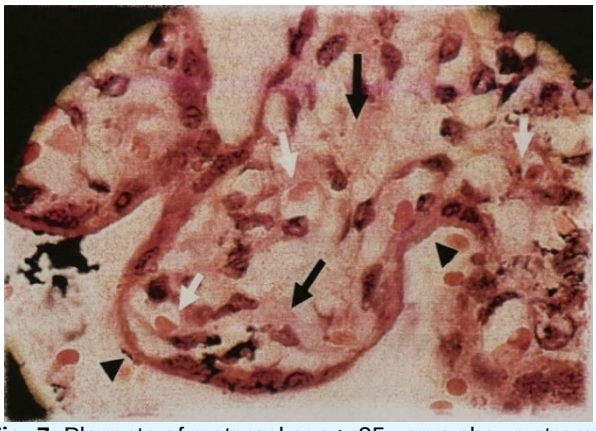

Fig. 7. Placenta of maternal age > 35 years shows stromal fibrosis (black arrows), small villous capillaries (white arrows), and thick placental barrier (black head arrows). X1000

placenta depends on welfare of the mother to whom it so intimately attached. This complex mother – placenta – fetus becoms very important in the whole process of development of the fetus. The placental basic histological structures undergo considerable changes throughout its lifespan. All the developmental changes need to be in accordance with its function (Gude et al. 2004). During pregnancy the normal changes happened in the shape of veins and arteries to follow the need of the fetus (Hansen 1986). Age of women has an important effect on the function of placenta during pregnancy and delivery (Hansen 1986). The risk of several types of antenatal, natal and delivery complications are more effect in older women during pregnancy (Frettis et al. 1995). Advanced maternal age defines as the age 35 years and older (Minoo et al. 2010). The placenta of mother < 35 years shows morphological changes which include increase in trophoblastic layer thickness, increase stroma fibrosis, decrease vascularization, more syncytial knots and low

incidence of apoptosis. Our findings reveal that there is a significant increase in the thickness of the placental barrier of mother > 35 years of age in regarding to normal group (p< 0.01) and (**Figs. 1** and **4**). These findings corroborate with the studies of (Zeno et al. 2011). It was noticed that there is an increase proliferative activity of trophoblast layer in the pregnant mother (20-34) years. Our finding may indicate that increase trophoblastic layer thickness in pregnant mother >35 years occur as a compensatory mechanism to allow the placenta provides nutrition for fetus for its normal physiological development. Our suggestion confirms the reported findings of (Mayhew 2004) that the increase in the proliferative activity occur in older women implies transport of substance through placenta is supported by compensatory mechanism and that help the placenta to meet the functional demands of fetus for the physiological growth and development. Our results support (Zlata et al. 2010) findings which show morphological changes of blood filled terminal villi which are important for feto-maternal transfer of the nutrient. It was noticed that there is an increase in the stromal tissue and decrease in the vascularization of the terminal villi in mothers >35 years in comparison to the control (20-34) years. Grebesa and Durest, (1994) showed in his study that total capillary surface area of placenta in old age women is lower in compare to placenta of younger pregnant mother. Ramic et al. (2006) had observed that the volume density of fibrinoid in older pregnant women compared to younger is significantly increase. These results goes with our study which shows decrease in vascularization of terminal villi and as a result there is increase in the stromal fibrosis of the placenta of the mother >35 years in comparison to placenta of control group as shown in (**Figs. 6** and **7**). Placental apoptosis which is a normal physiological phenomenon is increased largely as pregnancy progress (Smith et al. 2000). Qumsiyeh *et al*. (2000) have shown that apoptotic cells are more in younger age group compared with those from older age group. This finding is similar to our finding which shows more syncytial knots and high incidence of apoptosis in the control group in comparison to older age group as shown in **Figs. 4** and **5**. Toki et al. (1991) identify an inverse relationship between Be 1-2 family protein expression in syncytiotrophoblast, apoptosis and maternal age. Our results revealed that there is no significant differences in the mean birth weight of the babies of the two groups (p > 0.05) but there is significant increase in the mean placental weight as maternal age increase (p < 0.01) as in **Figs. 2** and **3**. Our results are in agreement with finding by Haavaldsen et al. (2001).

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